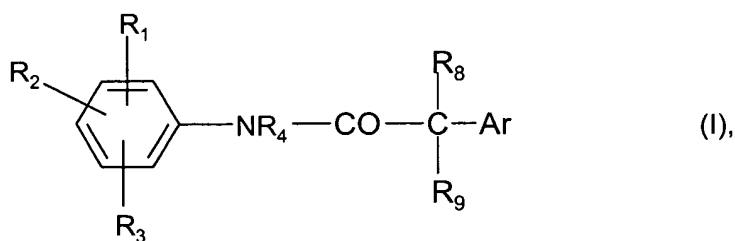


What is claimed is:

1. A carboxylic acid amide of the formula

5



wherein:

R₁ denotes a C₃₋₇-cycloalkyl-carbonyl group wherein

10

the methylene group in the 3 or 4 position in a C₅₋₇-cycloalkyl-carbonyl group may be replaced by an -NH group wherein

the hydrogen atom of the -NH group may be replaced by a C₁₋₃-alkyl, C₁₋₃-alkyl-carbonyl, phenylcarbonyl or phenylsulphonyl group,

15

a C₁₋₆-alkylcarbonyl group optionally terminally substituted in the alkyl moiety by an amino, C₁₋₃-alkylamino or di-(C₁₋₃-alkyl)-amino group,

a group of formula R_fR_gN-(CH₂)_m-(R_h)N-CO wherein

20

R_f, R_g and R_h independently of one another each denote a hydrogen atom or a C₁₋₃-alkyl group and

m denotes one of the numbers 2, 3, 4, 5 or 6,

a phenylcarbonyl, naphthylcarbonyl or heteroarylcarbonyl group,

25

a C₁₋₃-alkyl group monosubstituted by a hydroxy group or terminally disubstituted by a phenyl and a hydroxy group wherein

the phenyl substituent may be substituted by an amidino group optionally substituted by one or two C₁₋₃-alkyl groups, by a fluorine, chlorine or bromine atom, by a trifluoromethyl, C₁₋₃-alkyl or C₁₋₃-alkoxy group,

5

a 4- to 7-membered cycloalkyleneimino-carbonyl or cycloalkyleneimino-sulphonyl group substituted by an amino-C₁₋₃-alkyl, C₁₋₃-alkylamino-C₁₋₃-alkyl, di-(C₁₋₃-alkyl)-amino-C₁₋₃-alkyl, aminocarbonyl, C₁₋₃-alkylamino-carbonyl or di-(C₁₋₃-alkyl)-aminocarbonyl group,

10

a C₃₋₇-cycloalkylamino group which is substituted at the nitrogen atom by a C₁₋₃-alkyl-amino-C₁₋₃-alkyl or di-(C₁₋₃-alkyl)amino-C₁₋₃-alkyl group,

or, if R₂ denotes a trifluoromethyl group and/or R₅ denotes an amino-C₁₋₃-alkyl,

15

C₁₋₃-alkylamino-C₁₋₃-alkyl or di-(C₁₋₃-alkyl)amino-C₁₋₃-alkyl group and/or R₆ denotes a carboxy-C₁₋₃-alkoxy or C₁₋₄-alkoxy-carbonyl-C₁₋₃-alkoxy group and/or at least one of the groups R₈ or R₉ assumes a meaning other than the hydrogen atom, an unsubstituted 4- to 7-membered cycloalkyleneimino-carbonyl or cycloalkyleneimino-sulphonyl group, a C₃₋₇-cycloalkylamino or N-(C₁₋₃-alkyl)-C₃₋₇-cycloalkylamino group,

20

R₂ denotes a hydrogen, fluorine, chlorine or bromine atom, a C₁₋₃-alkyl group wherein the hydrogen atoms may be wholly or partly replaced by fluorine atoms, a hydroxy or C₁₋₃-alkoxy group,

25

R₃ denotes a hydrogen atom or a C₁₋₃-alkyl group,
R₄ denotes a hydrogen atom or a C₁₋₃-alkyl group optionally substituted by a carboxy group or a group which may be converted into a carboxy group in vivo,

Ar denotes a phenyl or naphthyl group substituted by the groups R₅, R₆ and R₇, while

30

R₅ denotes a cyano group, an amidino group optionally substituted by one or two C₁₋₃-alkyl groups, an amino-C₁₋₃-alkyl, C₁₋₃-alkylamino-C₁₋₃-alkyl or di-(C₁₋₃-alkyl)amino-C₁₋₃-alkyl group,

5 R₆ denotes a hydrogen, fluorine, chlorine or bromine atom, a trifluoromethyl, C₁₋₃-alkyl, hydroxy, hydroxy-C₁₋₃-alkyl, C₁₋₃-alkoxy, C₁₋₃-alkoxy-C₁₋₃-alkyl, carboxy, carboxy-C₁₋₃-alkyl, carboxy-C₁₋₃-alkoxy, C₁₋₄-alkoxy-carbonyl-C₁₋₃-alkoxy, phenyl-C₁₋₃-alkoxy, amino, C₁₋₃-alkylamino or di-(C₁₋₃-alkyl)amino group and

10 R₇ denotes a hydrogen, fluorine, chlorine or bromine atom or a C₁₋₃-alkyl group, or a thienylene, thiazolyne, pyridinylene, pyrimidinylene, pyrazinylene or pyridazinylene group optionally substituted in the carbon skeleton by a C₁₋₃-alkyl group,

15 R₈ and R₉, which may be identical or different, each denote a hydrogen atom, a C₁₋₃-alkyl group optionally substituted by a phenyl or heteroaryl group or an amino group optionally substituted by one or two C₁₋₃-alkyl or C₁₋₃-alkyl-carbonyl groups, while the term heteroaryl group mentioned above denotes a 5-membered heteroaryl group bound via a carbon or nitrogen atom which contains

20 an imino group optionally substituted by a C₁₋₄-alkyl or C₁₋₄-alkyl-carbonyl group, an oxygen or sulphur atom,

25 an imino group optionally substituted by a C₁₋₄-alkyl group or an oxygen or sulphur atom and additionally a nitrogen atom,

an imino group optionally substituted by a C₁₋₄-alkyl group and two nitrogen atoms or

30 an oxygen or sulphur atom and two nitrogen atoms,

or a 6-membered heteroaryl group which contains one or two nitrogen atoms,

while a phenyl ring may be fused to the abovementioned 5- or 6-membered heteroaryl groups via two adjacent carbon atoms and the bicyclic heteroaryl groups thus formed may be bound via the heteroaromatic or carbocyclic moiety,

and the unsubstituted or monosubstituted phenyl and naphthyl groups mentioned in the definition of the abovementioned groups, or the unsubstituted or monosubstituted phenyl and naphthyl groups contained in these groups, as well as the abovementioned heteroaryl groups may additionally be substituted at a carbon atom in each case by a fluorine, chlorine or bromine atom, by a trifluoromethyl, C₁₋₃-alkyl, C₁₋₃-alkoxy or C₁₋₃-alkoxy-carbonyl group, unless otherwise stated,

the carboxy groups mentioned in the definition of the abovementioned groups may be replaced by a group which may be converted *in vivo* into a carboxy group or by a group which is negatively charged under physiological conditions, and

the amino and imino groups mentioned in the definition of the abovementioned groups may be substituted by a group which can be cleaved *in vivo*,

and the compounds

2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-chloro-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-sulphonyl)-phenyl]-acetamide,

2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-bromo-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide and

2-(5-carbamidoyl-2-hydroxy-phenyl)-N-[3-methoxy-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

or a salt thereof.

5

2. A carboxylic acid amide of the formula I according to claim 1, wherein:

R₁ denotes a C₅₋₇-cycloalkyl-carbonyl group wherein the methylene group in the 3 or 4 position is replaced by an -NH group wherein

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the hydrogen atom may be replaced by a C₁₋₃-alkyl, C₁₋₃-alkyl-carbonyl or phenyl-carbonyl group,

a C₁₋₃-alkyl-carbonyl group optionally terminally substituted in the alkyl moiety by a

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C₁₋₃-alkylamino or di-(C₁₋₃-alkyl)-amino group,

a group of formula $R_f R_g N-(CH_2)_m-(R_h)N-CO$, wherein

R_f, R_g and R_h independently of one another each denote a hydrogen atom or a

20

C₁₋₃-alkyl group and

m denotes one of the numbers 2, 3 or 4,

a phenylcarbonyl or heteroarylcarbonyl group,

25

while the heteroaryl moiety contains a 6-membered heteroaryl group which contains one or two nitrogen atoms and to which a phenyl ring may be fused via two adjacent carbon atoms, while the bicyclic heteroaryl groups thus formed may be bound via the heteroaromatic or carbocyclic moiety, e.g. a 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, quinolinyl, isoquinolinyl, quinoxalinyl or

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quinazolinyl group,

a C₁₋₃-alkyl group monosubstituted by a hydroxy group or terminally disubstituted by a phenyl group and a hydroxy group wherein

the phenyl substituent may be substituted by an amidino group optionally substituted
 5 by one or two C₁₋₃-alkyl groups, by a fluorine, chlorine or bromine atom, by a trifluoromethyl, C₁₋₃-alkyl or C₁₋₃-alkoxy group,

a 4- to 7-membered cycloalkyleneimino-carbonyl group substituted by an amino-C₁₋₃-alkyl, C₁₋₃-alkylamino-C₁₋₃-alkyl, di-(C₁₋₃-alkyl)-amino-C₁₋₃-alkyl,
 10 C₁₋₄-alkoxy-carbonyl-amino-C₁₋₃-alkyl, aminocarbonyl, C₁₋₃-alkylamino-carbonyl or di-(C₁₋₃-alkyl)-aminocarbonyl group,

a C₅₋₇-cycloalkylamino group which is substituted at the nitrogen atom by a C₁₋₃-alkyl-amino-C₁₋₃-alkyl or di-(C₁₋₃-alkyl)amino-C₁₋₃-alkyl group,

15 or, if R₂ denotes a trifluoromethyl group and/or R₅ denotes an amino-C₁₋₃-alkyl or C₁₋₃-alkylamino-C₁₋₃-alkyl group and/or R₆ denotes a carboxy-C₁₋₃-alkoxy or C₁₋₄-alkoxy-carbonyl-C₁₋₃-alkoxy group and/or at least one of the groups R₈ or R₉ assumes a meaning other than the hydrogen atom, an unsubstituted 4- to 7-membered
 20 cycloalkyleneiminocarbonyl group, a C₅₋₇-cycloalkylamino or N-(C₁₋₃-alkyl)-C₅₋₇-cycloalkylamino group,

R₂ denotes a hydrogen, fluorine, chlorine or bromine atom, a C₁₋₃-alkyl, trifluoromethyl or C₁₋₃-alkoxy group,

25 R₃ denotes a hydrogen atom or a C₁₋₃-alkyl group,

R₄ denotes a hydrogen atom or a C₁₋₃-alkyl group,

30 Ar denotes a phenyl group substituted by the groups R₅ and R₆ wherein

R₅ denotes a cyano group, an amidino group optionally substituted by one or two C₁₋₃-alkyl groups, an amino-C₁₋₃-alkyl or C₁₋₃-alkylamino-C₁₋₃-alkyl group and

R₆ denotes a hydrogen, fluorine, chlorine or bromine atom, a trifluoromethyl, C₁₋₃-alkyl, hydroxy, C₁₋₃-alkoxy, carboxy-C₁₋₃-alkoxy or C₁₋₄-alkoxy-carbonyl-C₁₋₃-alkoxy group, and

R₈ and R₉, which may be identical or different, each denote a hydrogen atom, a C₁₋₃-alkyl group optionally substituted by an phenyl or pyridinyl group or an amino group optionally substituted by one or two C₁₋₃-alkyl or C₁₋₃-alkyl-carbonyl groups,

while the unsubstituted or monosubstituted phenyl groups mentioned in the definition of the abovementioned groups, or the unsubstituted or monosubstituted phenyl moieties contained in these groups, as well as the abovementioned heteroaryl groups may additionally be substituted at a carbon atom in each case by a fluorine, chlorine or bromine atom, by a trifluoromethyl, C₁₋₃-alkyl, C₁₋₃-alkoxy or C₁₋₃-alkoxy-carbonyl group, unless otherwise stated,

and the compounds

2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-chloro-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-sulphonyl)-phenyl]-acetamide,

2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-bromo-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide and

2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methoxy-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

or a salt thereof.

3. A carboxylic acid amide of the formula I according to claim 1, wherein:

5

the groups R₁ to R₄, R₈ and R₉ are defined as in claim 1 or 2, but R₁ in the 4 position is bound to the phenyl group contained in formula I and

Ar denotes a phenyl group disubstituted by the groups R₅ and R₆, while

10

R₅ is bound in the 3 position if R₆ denotes a hydrogen atom, or is bound in the 5 position if R₆ assumes a meaning other than the hydrogen atom, and an amidino group optionally substituted by one or two C₁₋₃-alkyl groups, an amino-C₁₋₃-alkyl or C₁₋₃-alkylamino-C₁₋₃-alkyl group and

15

R₆ denotes a hydrogen atom or a trifluoromethyl, C₁₋₃-alkyl, hydroxy, C₁₋₃-alkoxy, carboxy-C₁₋₃-alkoxy or C₁₋₄-alkoxy-carbonyl-C₁₋₃-alkoxy group bound in the 2 position,

20 and the compounds

2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-chloro-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide and

25

2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-bromo-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

or a salt thereof.

30

4. A carboxylic acid amide of the formula I according to claim 1, wherein:

R₁ is bound in the 4 position of the phenyl group of formula I and denotes

a C₅₋₇-cycloalkyl-carbonyl group wherein the methylene group in the 3 or 4 position is replaced by an -NH group,

5

a phenylcarbonyl or pyridylcarbonyl group optionally substituted by a fluorine, chlorine or bromine atom or by a C₁₋₃-alkyl group,

a C₁₋₃-alkyl group terminally disubstituted by a phenyl and a hydroxy group wherein

10

the phenyl substituent may be monosubstituted by a C₁₋₃-alkyl or an amidino group or may be disubstituted by a C₁₋₃-alkyl and an amidino group,

a 5- to 7-membered cycloalkyleneimino-carbonyl group substituted by an

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amino-C₁₋₃-alkyl, C₁₋₃-alkylamino-C₁₋₃-alkyl, C₁₋₄-alkoxy-carbonyl-amino-C₁₋₃-alkyl, aminocarbonyl or C₁₋₃-alkylamino-carbonyl group,

or, if R₂ denotes a trifluoromethyl group and/or R₅ denotes an amino-C₁₋₃-alkyl group

and/or R₆ denotes a carboxy-C₁₋₃-alkoxy or C₁₋₄-alkoxy-carbonyl-C₁₋₃-alkoxy group and/or

20

at least one of the groups R₈ or R₉ assumes a meaning other than the hydrogen atom, an unsubstituted 5- to 7-membered cycloalkyleneimino-carbonyl or cycloalkyleneimino-sulphonyl group and

R₂ denotes a hydrogen atom or a substituent bound in the 3 position of the phenyl group,

25

selected from among fluorine, chlorine, bromine, C₁₋₃-alkyl, C₁₋₃-alkoxy and trifluoromethyl,

R₃ and R₄ each denote a hydrogen atom,

30

Ar denotes a phenyl group substituted by the groups R₅ and R₆ wherein

R₅ is bound in the 3 position if R₆ denotes a hydrogen atom, or is bound in the 5 position if R₆ assumes a meaning other than the hydrogen atom, and an amidino or amino-C₁₋₃-alkyl group and

- 5 R₆ denotes a hydrogen atom or a hydroxy, C₁₋₃-alkoxy, carboxy-C₁₋₃-alkoxy or C₁₋₄-alkoxy-carbonyl-C₁₋₃-alkoxy group bound in the 2 position, and

10 R₈ and R₉, which may be identical or different, each denote a hydrogen atom, a C₁₋₃-alkyl group optionally substituted by a phenyl, 4-(C₁₋₃-alkoxy-carbonyl)-phenyl or pyridinyl group or an amino group optionally substituted by one or two C₁₋₃-alkyl or C₁₋₃-alkyl-carbonyl groups,

and the compounds

- 15 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-chloro-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide and

2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-bromo-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

20

or a salt thereof.

5. A compound selected from the group consisting of:

- 25 (1) (L)-2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(2-aminocarbonyl-pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

(2) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-{3-methyl-4-[2-(tert.butoxycarbonyl-aminomethyl)-piperidin-1-yl-carbonyl]-phenyl}-acetamide,

30

(3) 2-(5-aminomethyl-2-hydroxy-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

(4) 2-(3-carbamimidoyl-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-
5 isobutyramide,

(5) 2-(5-carbamimidoyl-2-ethoxycarbonylmethyloxy-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

10 (6) 2-(5-carbamimidoyl-2-carboxymethyloxy-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

(7) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(piperidin-3-yl-carbonyl)-phenyl]-acetamide,

15 (8) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-(3-methyl-4-benzoyl-phenyl)-acetamide,

(9) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(1-hydroxy-1-phenyl-methyl)-phenyl]-acetamide,

20 (10) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-{4-[1-(3-carbamimidoyl-phenyl)-1-hydroxy-methyl]-3-methyl-phenyl}-acetamide,

→ (11) 2-(3-carbamidoyl-phenyl)-N-[3-methyl-4-(pyridin-3-yl-carbonyl)-phenyl]-
25 isobutyramide,

(12) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-isobutyramide,

30 (13) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-chloro-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,

- (14) 2-(3-carbamimidoyl-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-2-amino-acetamide,
- 5 (15) 2-(3-carbamimidoyl-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-2-(acetylamino)-acetamide,
- (16) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-sulphonyl)-phenyl]-acetamide,
- 10 (17) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-propionamide,
- (18) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-trifluoromethyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,
- 15 (19) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[4-(pyrrolidin-1-yl-carbonyl)-3-trifluoromethyl-phenyl]-propionamide,
- (20) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-bromo-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,
- 20 (21) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-bromo-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-propionamide,
- 25 (22) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methoxy-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide,
- (23) 2-(3-carbamimidoyl-phenyl)-N-[3-bromo-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-3-phenyl-propionamide,
- 30

(24) 2-(3-carbamimidoyl-phenyl)-N-[3-bromo-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-3-(pyridin-4-yl)-propionamide and

(25) 2-(3-carbamimidoyl-phenyl)-N-[3-bromo-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-3-[4-(ethoxycarbonyl)-phenyl]-propionamide,

or a derivative thereof wherein at least one amidino group is substituted by a C₁₋₆-alkoxy-carbonyl or phenylcarbonyl,

or a salt thereof.

6. A physiologically acceptable salt of a compound according to claim 1, 2, 3, 4 or 5, with the exception of those compounds wherein Ar denotes a phenyl or naphthyl group substituted by the groups R₅, R₆ and R₇, and R₅ denotes a cyano group.

7. A pharmaceutical composition comprising a compound in accordance with claim 1, 2, 3 or 4, with the exception of those compounds wherein Ar denotes a phenyl or naphthyl group substituted by the groups R₅, R₆ and R₇ and R₅ denotes a cyano group, or a physiologically acceptable salt thereof, together with one or more inert carriers and/or diluents.

8. A method for treating thrombus formation which method comprises administering to a host in need of such treatment an antithrombotic amount of a compound in accordance with claim 1, 2, 3 or 4, with the exception of those compounds wherein Ar denotes a phenyl or naphthyl group substituted by the groups R₅, R₆ and R₇ and R₅ denotes a cyano group, or a physiologically acceptable salt thereof.